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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/812,633	03/19/2001	Thomas L. Benjamin	00742/066001	1354
21559	7590	12/17/2003	EXAMINER	
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			LI, QIAN JANICE	
			ART UNIT	PAPER NUMBER
			1632	
DATE MAILED: 12/17/2003				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	09/812,633	BENJAMIN ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 15 September 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-52 is/are pending in the application.
- 4a) Of the above claim(s) 13-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 March 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

### DETAILED ACTION

The amendment, response, and the Declaration submitted in June 2003, and the supplemental amendment filed on 9/15/03 have been entered. Claims 1 and 7 have been amended. Claims 1-12 are under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment will not be reiterated. The arguments in the response would be addressed to the extent that they apply to current rejection.

This application contains claims (13-52) drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

#### WRITTEN DESCRIPTION REQUIREMENT

Claims 1-12 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue they have found more than one point mutation, and submitted a Declaration and exhibits to support the arguments.

The arguments, Declaration, and exhibits have been fully considered but they are not persuasive for supporting the full scope of the claims.

In exhibit I, applicants presented multiple mutated or polymorphic alleles found in p150<sup>Sal2</sup> gene in ovarian tumors, however, they are all coding sequence point mutations. Out of the seven listed alterations, only the heterozygous S/P and homozygous P/P are present *exclusively* in tumor tissues, which shows a tumor relevance (which is not in the application as original filed), the rest of the polymorphism are present in both normal tissue and tumor tissue (including the original disclosed S73C and G744R), and the specification fails to teach which of these alterations are proliferative disease-associated, thus the relevance of the alterations with the risk of acquiring a tumor is uncertain. Further, the detected change is characterized by point mutation in the cDNA, whereas the claims encompass any changes in a *Sal2* gene, such as gene silencing due to regulatory alteration, and locus rearrangement in genomic sequences, which the specification clearly teaches that such has not been found (Specification, page 36, lines 7-10). Thus, the disclosure fails to support the full scope of the claims.

In exhibit II, applicants submitted tests conducted in samples from colon cancer and kidney tumors in addition to the originally presented ovarian tumors. However, the data are all drawn to a malignant proliferation, whereas the claims encompassing any proliferative diseases such as restenosis, the specification and the supplemental data

failed to present any data showing that the change in p150<sup>Sal2</sup> gene is associated with any benign proliferative disease, thus, the disclosure fails to support the full scope of the claims.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of "a proliferative disease-associated alteration in Sal2 nucleic acid".

Claims 1-12 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record and following.

As an initial matter, it is noted that arguments drawn to detection of abnormal Sal2 proteins are moot because the elected invention for examination is identifying a mammal having or at risk of acquiring a proliferative disease by determining whether there is a proliferative disease-associated alteration in a Sal2 nucleic acid in a mammal.

Applicants pointed to figure 7, table 3, and the Declaration as the enablement support for instantly claimed invention. However, figure 7, table 3, exhibits I & II of the Declaration are all drawn to detecting alterations in the p150<sup>Sal2</sup> protein, none of these illustrations utilizes a *nucleic acid* detection method. Moreover, the specification particularly teaches "*no evidence of loss or gross rearrangement of the hSal2 locus was seen in any of the tumors examined*", the sequences from two tumors 327 and 523 that are negative for p150<sup>sal2</sup> expression, "*showed sequences identical to published genomic*

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*sequence [of hSal2] (1<sup>st</sup> & 2<sup>nd</sup> paragraphs in page 36). The specification goes on to teach, "the absence of p150<sup>Sal2</sup> expression in a majority of ovarian cancers may reflect mechanisms other than loss of the hSal2 itself, such as silencing of expression through promoter methylation, alterations in an upstream regulatory factor, or factors leading to instability of the protein itself" (lines 7-10, page 36). Apparently, neither the specification nor the supplemental disclosure teaches a proliferative disease-associated alteration in a Sal2 nucleic acid has been detected via nucleic acid detection approach. Accordingly, the specification fails to provide an enabling disclosure for the skilled intending to practice the invention as it is now claimed.*

Moreover, the disclosure fails to provide a requisite standard for identifying a mammal having or at increased risk of acquiring a proliferative disease from the alteration(s) of Sal2 nucleic acid because most of the mutations or polymorphic alleles are present in both normal and abnormal tissue. The specification fails to teach when such a mutation is detected in a normal individual, how to determine whether it is disease-associated. The skilled artisan would not know how to predictably determine whether the subject is at risk of developing a cancer since it could occur in both health and disease.

Accordingly, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

### **Conclusion**

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942 (571-272-0730, after the Office relocation in January, 2004). The examiner can normally be reached on 9:30 am - 6 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Q. Janice Li  
Patent Examiner  
Art Unit 1632

*QJL*

December 15, 2003

**ANNIE M. WEHBE' PH.D**  
**PRIMARY EXAMINER**

*Allee*